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Characteristics of a cohort of high-risk men who have sex with men on pre-exposure prophylaxis reporting transgender sexual partners

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Abstract

Transgender people continue to be at high-risk for HIV acquisition, but little is known about the characteristics of their sexual partners. To address this gap, we examined sociodemographic and sexual characteristics of cisgender men who have sex with men (MSM) on pre-exposure prophylaxis (PrEP) reporting transgender sexual partners.

A cohort of 392 MSM in southern California in a randomized clinical trial for PrEP adherence were followed from 2013 to 2016. Multivariable generalized estimating equation and logistic models identified characteristics of MSM reporting transgender sexual partners and PrEP adherence.

Only 14 (4%) MSM reported having transgender sexual partners. MSM were more likely to report transgender partners if they were African American, had incident chlamydia, reported injection drug-using sexual partners, or received items for sex. Most associations remained significant in the multivariable model: African American (adjusted odds ratio [AOR] 11.20, $P = .01$), incident chlamydia (AOR 3.71, $P = .04$), and receiving items for sex (AOR 5.29, $P = .04$). There were no significant differences in PrEP adherence between MSM reporting transgender partners and their counterpart.

MSM who report transgender sexual partners share characteristics associated with individuals with high HIV prevalence. Identifying this group distinct from larger cohorts of MSM could offer new HIV prevention opportunities for this group of MSM and the transgender community.

Abbreviations: AOR = adjusted odds ratio, CASI = computer assisted self-interviewing, GEE = generalized estimating equations, IDU = injection drug use, IQR = interquartile range, MSM = men who have sex with men, OR = odds ratio, PrEP = pre-exposure prophylaxis, RPR = rapid plasma regain, STI = sexually transmitted infection, TAPIR = Text Messaging to Improve Adherence to PrEP in Risky MSM, TFV-DP = tenofovir diphosphate, TGM = transgender men, TGW = transgender women.

Keywords: female to male, HIV risk factors, male to female, men who have sex with men, PrEP, transgender

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1. Introduction

While overall incidence of HIV in the United States (US) have been on a decline, cisgender men who have sex with men (MSM) and transgender people, individuals whose gender identity and/or expression is different from their sex assigned at birth,^[1] continue to be at high risk of HIV acquisition. In 2016, MSM aged 13 years and older accounted for 67% of new HIV diagnoses in the United States.^[2] Transgender people had 3 times the national average of new HIV diagnosis in 2015, with over 5 times as many HIV diagnosis in transgender women (TGW) than in transgender men (TGM).^[3] A recent systemic review and meta-analysis among US transgender population, estimated to comprise of 1 million adults,^[4] reported that the prevalence of lab confirmed HIV infection was 9% (95% CI 6–14%), whereas self-reported HIV infection was 16% (95% CI 12–21%).^[5]

MSM^[6] and transgender people^[7] have both self-identified cisgender and transgender sexual partners, adding complexity in identifying risk factors based on sexual partner types. Individual risks of HIV acquisition for MSM have been associated with condomless anal receptive sex, high frequency of male partners, injection drug use (IDU), high viral load in index partner, and amphetamine type stimulants.^[8] Individual risks of HIV acquisition for transgender people are similar to those of MSM and have been associated with condomless anal sex, multiple casual partner, sex work, IDU, mental health concerns,

and economic marginalization.^[5,9,10] Research on TGM is limited, but has found TGM often identify as “gay” and also engage in high HIV acquisition risk behaviors including both anal and vaginal intercourse.^[11] However, individual risk factors are insufficient to understand the network-level transmission between MSM and transgender people. Furthermore, TGM report different risk behaviors in the context of primary and concurrent partners outside their primary relationship.^[12] The intersection of social and gender identities and different contextual risk between transgender people and their sexual partners make it difficult to appropriately target and design HIV interventions and prevention strategies.^[13]

Current risks associated with sexual partners of transgender people include condomless sex and substance use, including poppers and methamphetamine.^[12,14] More specifically, African American MSM with transgender partners are 3 times more likely to have at least 5 new recent sexual partners and twice as likely to have condomless sexual acts.^[15] African American MSM with transgender partners were also found to be older, have a history of incarceration and identified their sexual orientation as “other than homosexual”.^[15] To further understand the characteristics distinguishing sexual partners of transgender people, we used data from a cohort of high-risk HIV-uninfected cis-MSM enrolled in a pre-exposure prophylaxis (PrEP) adherence trial to identify risk factors associated with having a transgender partner. We hypothesized that cis-MSM reporting a transgender partner over the 48-week study would be associated with higher risk behaviors compared with their counterparts.

2. Methods

2.1. Design and setting

This study is a secondary analysis of 392 cis-MSM (hereon referred to as MSM) at increased risk of HIV followed for 48 weeks from February 2013 through March 2016 as part of the Text Messaging to Improve Adherence to PrEP in Risky MSM (TAPIR) study in 4 Southern California medical centers located in San Diego, Los Angeles, and Long Beach. Design and eligibility of the TAPIR study is described in detail elsewhere.^[16] Data for this analysis includes sociodemographic characteristics collected at baseline; sexual and risk behavior characteristics reported at weeks 0, 4, 12, 24, 36, and 48 using a computer assisted self-interviewing (CASI) survey; and laboratory sexually transmitted infection (STI) testing at baseline and every 12 to ~24 weeks.

2.2. Variables of interest

The longitudinal dependent variable of having a transgender sexual partner (TGW and/or TGM) was captured by asking participants in the sexual risk questionnaire, “In the past 3 months who did you have sex with?” Those who responded to either “male to female transgender” or “female to male transgender” were considered to have a transgender sexual partner. Ever having a transgender sexual partner was defined as having reported a transgender partner at least once over the 48 weeks of CASI assessments.

Assessment of independent variables included socioeconomic status (e.g., age, race/ethnicity, annual income, and education level), drug use (e.g., alcohol, marijuana, poppers, dissociatives, hallucinogens, cocaine, and methamphetamine), and sexual risk behavior in the past 3 months, which was captured from structured CASI questionnaires. Participants indicating a male

and/or transgender sex partner in the past 3 months were also asked for:

- (1) Number of male partners;
- (2) Engagement in anal insertive or anal receptive sex and frequency of condom use for anal insertive or anal receptive sex;
- (3) Receipt of money, drugs or items for sex;
- (4) Partner HIV status (positive or unknown); and
- (5) Partner who is an IDU.

Response options were categorized to best accommodate the limited number of outcomes.

2.3. Biomedical factors

STI screening assessments were conducted for syphilis using serum rapid plasma regain (RPR) and confirmatory treponemal test, and for chlamydia and gonorrhea of urine, pharynx and rectum using Hologic Aptima Combo2. Lab results for gonorrhea and chlamydia were dichotomized for a positive rectal, urine, or pharyngeal test and for new syphilis for a positive RPR upon clinical verification. PrEP adherence was measured by dried blood spot tenofovir diphosphate (TFV-DP) concentrations (fmol/punch) at weeks 12 and 48 using liquid chromatography-tandem mass spectrometry assay validated for determination of TFV in human red blood cells.^[17] Adherence was considered adequate if TFV-DP levels were >719 fmol/punch (≥ 4 doses/week) and perfect if >1246 fmol/punch (7 doses/week) with thresholds verified previously.^[17]

2.4. Statistical analysis

Baseline characteristics were summarized by MSM ever reporting a transgender partner using simple frequencies. Pearson’s chi-squared compared differences in frequencies and proportions for categorical variables and Fisher’s exact method when cell frequencies were <5 . As the TAPIR study was prospective and sexual behavior may be non-independent within participants over time, marginal risk factors associated with reporting a transgender partner were estimated using a generalized estimating equations (GEE) under a binomial distribution with a logit link model. Robust estimates of standard errors were applied based on the sandwich estimator with an exchangeable working correlation matrix for valid estimates. Missing data assumption of missing completely at random was tested using Little’s X^2 test. As PrEP was initiated at enrollment, the GEE model included data from weeks 4 to 48 adjusted for race/ethnicity, incident chlamydia, IDU sex partner, and receiving items for sex selected based on significance of $P < .05$ on the univariate model. For analytical purposes, number of male sexual partners was square root transformed to adjust for skewness and ease of interpretability. Association between PrEP adherence and reporting a transgender partner was modeled using logistic regression adjusted for race/ethnicity, education, receipt of money, drugs or items for sex, and sex with HIV unknown, positive or IDU partner, selected a priori. Data management and statistical analysis was conducted using STATA/SE 15.1, StataCorp LP, College Station, TX.

2.5. Ethics approval and consent to participate

The main TAPIR study was approved and performed as per regulations by University of California San Diego Human

Research Protections Program, Los Angeles BioMedical Research Institute at Harbor-UCLA Medical Center Institutional Review Board and University of Southern California Office for the Protection of Research Subjects. The study was registered with ClinicalTrials.gov (NCT01761643) on January 2013 and explained to all volunteers including purpose, procedures and risks and benefits of participating before seeking a written informed consent.

3. Results

3.1. MSM characteristics at baseline

The median age of 392 participants was 33 years (interquartile range [IQR]: 28–41) with the majority being White (50%) and Hispanic (30%), with fewer African American and Asian, multi, or other race. Among MSM ever reporting a transgender partner, 43% (6 of 14) were African American compared to only 10% (38 of 378) of MSM who never reported a transgender partner ($P=.001$). Sixty-four percent (9 of 14) of MSM earned an annual income of at least \$24,000 and had some college or higher education. Seventy-two percent (10 of 14) used some drugs at baseline, alcohol was the most popular (64%). Twenty-one percent (3 of 14) of participants had a STI (gonorrhea, chlamydia, and/or syphilis) at baseline. There were no significant differences in age, income, education, drug use, and STI between MSM reporting transgender partners compared with MSM never reporting transgender partners at baseline. MSM reporting a transgender partner were more likely to have sex partners who reported IDU (36% vs 13%, $P=.02$) or of unknown HIV status (86% vs 55%, $P=.03$) compared to those with no transgender partners (Table 1).

3.2. MSM characteristics over time

Of 392 MSM included in this study, 14 (4%) reported having at least 1 transgender sexual partner in the last 3 months over the 48 weeks study period. Nine MSM reported having only TGW as sexual partners, 3 reported having only TGM sexual partner, and 2 reported both TGW and TGM as sexual partners. In univariate analysis, MSM who were African American and Asian/multi/other MSM had higher odds of reporting a transgender partner (Table 2). Sexual risk factors associated with reporting a transgender partner were incident chlamydia (odds ratio [OR] 3.41, $P=.04$), engaging with an IDU sex partner (OR 4.67, $P=.01$) and receiving money or other items for sex (OR 6.77, $P=.001$). Controlling for confounders, African American (adjusted odds ratio [AOR] 11.20, $P=.01$) MSM were more likely to report transgender partners compared with White MSM. MSM with incident chlamydia (AOR: 3.71, $P=.04$) and receiving items in exchange for sex (AOR 5.29, $P=.04$) remained significant in the adjusted model and were more likely to report transgender partners. Having a sex partner who used injection drugs was not significant in the adjusted model.

3.3. PrEP adherence

Adherence to PrEP at week 12 was measured for 355 participants, 37 participants, including 4 MSM with transgender partners did not have any adherence results. Among 355 participants with complete results, 319 (90%) had adequate or perfect adherence (Table 3). Seventy percent (7 of 10) of MSM reporting transgender partners had adequate/perfect adherence

compared with 90% (309 of 345) of MSM without a transgender partner (OR 0.27, $P=.06$). Similarly, adherence levels at week 48 between the 2 groups showed non-significant results.

4. Discussion

In our cohort of HIV-negative MSM on PrEP in southern California, several factors were associated with having a transgender sexual partner including African American race, incident chlamydia infection, and having partners engaging in high HIV risk behaviors such as IDU and receipt of money, drugs, or items in exchange for sex. We found no difference in PrEP adherence between those reporting transgender partners and those without transgender partners.

Given the high rates of new HIV infection among African American MSM,^[18–20] our finding that African American MSM were more likely to report having a transgender partner compared to White MSM is consistent with there being a higher risk sexual network for transgender people. Previous work examining sexual partner characteristics similarly found that HIV-positive partners of TGW were more likely to be African American and identify as MSM.^[21] In a 2014 San Francisco study of MSM and TGW,^[22] African American MSM and TGW were overall more similar in socioeconomic status compared with White MSM, suggesting race/ethnicity and socio-economic status may be driving forces in establishing this sexual network. Looking at HIV diagnoses among African American MSM by age group, there was an overall decrease in HIV diagnoses in all age groups except for 25–34-year category which showed a 40% increase between 2010 and 2016.^[23] Interestingly, according to a 2010 HPTN cohort, African MSM most likely to report a transgender partner were ≥ 46 years of age (AOR 1.69, 95% CI 1.22–2.35).^[15] It appears that although young African American MSM experience the greatest burden of the HIV epidemic, older African American MSM with stable HIV diagnoses are more likely to report a transgender partner.^[23]

In addition to sociodemographic characteristics, transgender people have reported high risk behaviors including condomless anal receptive sex, STIs, and sex work in previous and current studies.^[7,24–27] We found similar trends in our cohort of MSM including chlamydia infections, having sex partners who use injection drugs, and receiving money or other items in exchange for sex. Despite the relatively small numbers that may have affected these aforementioned factors, chlamydia infections and receiving money or other items in exchange for sex remained significant in the adjusted model. Engaging in exchange sex has consistently been reported as more frequent among transgender people.^[21,28,29] MSM on PrEP in this study with transgender partners also share this high-risk behavior. Molecular epidemiology on the HIV-1 transmission network of TGW using genetic sequencing show TGW to cluster with other TGW and cis-men, further suggesting high risk activities and partners are shared between these groups.^[30] Shared risk behaviors make it imperative to target both transgender people and their MSM partners separate from larger cohorts of MSM as part of the sexual network that facilitate transmission between these 2 risk groups. However, identifying MSM who have transgender partners is challenging due to discordance between men's sexual identity and sexual behavior^[31]; MSM who report TGM as sexual partners may not identify as MSM. In a cohort of African American MSM, 90% with transgender partners did not identify

Table 1**Demographic and behavioral characteristic of HIV-uninfected cis-MSM at baseline.**

	Transgender sexual partner ever						Transgender sexual partner ever				
	No (N = 378)		Yes (N = 14)		P		No (N = 378)		Yes (N = 14)		P
	n	%*	n	%*			n	%*			
Demographics											
Race/ethnicity					.001	Education					.21
White	194	51	2	14		High school or less	31	8	3	21	
Hispanic	112	30	4	29		College	268	71	9	64	
Asian/multi/other	34	9	2	14		Advanced degree	79	21	2	14	
African American	38	10	6	43							
Age					.37	Annual income					.63
19–29	121	32	6	43		<\$24,000	79	21	4	28	
30–39	152	40	3	21		≥ \$24,000	238	63	9	64	
40+	105	28	5	36							
Drug use											
Any drug use					1.0	Illegal activity for drugs					1.00
No	100	27	4	29		No	347	92	13	93	
Yes	277	73	10	72		Yes	30	8	1	7	
Alcohol					1.00	Poppers					.28
No	65	17	2	14		No	180	48	9	64	
Yes	312	83	12	86		Yes	197	52	5	36	
Marijuana					.28	Multiple drug use†					.12
No	198	52	5	36		No	138	37	8	57	
Yes	179	47	9	64		Yes	239	63	6	43	
Sexual risk behavior											
No. male sex partners, median (IQR)	6	3, 10	12	4, 25	.09	Douching/enema					.40
						No	122	32	6	43	
						Yes	253	67	8	57	
AI sex with male partner					1.00	AR sex with male partner					.72
No	46	12	1	7		No	85	23	3	21	
Yes	321	85	10	71		Yes	284	75	8	57	
Condom use for AI sex					.84	Condom use for AR sex					1.00
Never	61	16	1	7		Never	43	11	1	7	
Rarely/sometimes	161	43	5	36		Rarely/sometimes	120	32	3	21	
Often/always	100	27	4	29		Often/always	120	32	4	29	
Buy sex‡					.53	Sell sex§					.35
No	359	95	13	93		No	346	91	12	86	
Yes	19	5	1	7		Yes	32	9	2	14	
Method for meeting sexual partner					.27	Sex partner – HIV status unknown					.027
None	43	11	1	7		No	170	45	2	14	
Online app	122	32	2	14		Yes	208	55	12	86	
Bathhouse/bar/combo	210	56	11	79							
Sex partner – injection drug use					.017	Sex partner – HIV positive					.78
No	328	87	9	64		No	123	33	5	36	
Yes	50	13	5	36		Yes	255	67	9	64	
Sexually transmitted infections											
Any STI (GC/CT/Syp)					1.00	Gonorrhea					1.00
No	300	80	11	79		No	338	89	13	93	
Yes	77	20	3	21		Yes	40	11	1	7	
Syphilis					1.00	Chlamydia					.40
No	376	99	14	100		No	332	88	11	79	
Yes	1	1	0	0		Yes	46	12	3	21	

AI = anal insertive, AR = anal Receptive, CT = chlamydia, GC = gonorrhea, IQR = interquartile range, MSM = men who have sex with men, STI = sexually transmitted infection, Syp = syphilis.

*Percent may not total 100 because of missing data/rounding.

† Any use of poppers, methamphetamine, dissociatives, hallucinogens, and/or cocaine.

‡ Give money/items/drugs for sex.

§ Receive money/items/drugs for sex.

as homosexual^[15] and MSM identifying as bisexual receive stigmatizing or negative attitude, making it less attractive to disclose gender identity.^[32] Continuing efforts to minimize disparities in social attitudes towards bisexual men and women

while affording participants to report non-binary gender and sexual identities would benefit future research.

Our study specifically identified risk behaviors for MSM with transgender partners on PrEP, which reduces HIV transmission

Table 2**Adjusted/unadjusted odds of reporting a transgender sexual partner among HIV-uninfected cis-MSM on PrEP.**

Characteristic	Reported ≥1 transgender sexual partner					
	Univariate			Multivariate		
	OR	95% CI	P	AOR*	95% CI	P
<i>Demographics</i>						
Age						
19–29	Ref	—	—			
30–39	0.40	0.09–1.85	0.240			
40+	1.01	0.26–3.97	0.989			
Race						
White	Ref	—	—	Ref	—	—
Hispanic	4.16	0.66–26.28	0.130	3.13	0.53–18.37	0.207
Asian/multi/other	9.09	1.21–68.07	0.032	7.10	0.62–81.65	0.116
African American	13.69	2.77–70.37	0.002	11.20	1.65–76.14	0.014
Annual income						
<\$24,000	Ref	—	—			
≥ \$24,000	0.55	0.15–1.95	0.352			
Education						
High school or less	2.58	0.51–13.06	0.252			
Some college	—	—	—			
Some advanced degree	0.63	0.13–3.03	0.568			
Drug and STI						
Multiple drug use [†]						
No	Ref	—	—			
Yes	0.64	0.19–2.10	0.459			
Incident chlamydia [‡]						
No	Ref	—	—	Ref	—	—
Yes	3.41	1.06–10.97	0.040	3.71	1.06–12.98	0.040
Incident gonorrhea [‡]						
No	—	—	—			
Yes	3.27	0.76–14.12	0.113			
Sexual risk behavior						
Sex partner – injection drug use						
No	Ref	—	—	Ref	—	—
Yes	4.67	1.39–15.71	0.013	2.78	0.59–13.09	0.195
Sex partner – HIV status unknown						
No	Ref	—	—			
Yes	1.99	0.67–5.92	0.212			
Receive money/items/drugs for sex						
No	Ref	—	—	Ref	—	—
Yes	6.77	2.14–21.34	0.001	5.29	1.04–26.87	0.045
Method of meeting partner						
None	Ref	—	—			
Internet/mobile app only	1.11	0.24–5.15	0.891			
Bath house/bar/combo	1.61	0.44–5.81	0.471			
Number of male sex partners [§]	1.28	0.98–1.66	0.067			
Condom use for anal insertive sex						
Never	3.14	0.61–16.14	0.172			
Rarely/sometimes	0.66	0.09–4.80	0.682			
Often/always	Ref	—	—			
Condom use for anal receptive sex						
Never	1.60	0.27–9.61	0.606			
Rarely/sometimes	0.34	0.03–3.74	0.377			
Often/always	Ref	—	—			

AOR=adjusted odds ratio, CI=confidence interval, IDU=injection drug use, MSM=men who have sex with men, OR=odds ratio, PrEP=pre-exposure prophylaxis.

* Adjusted for race/ethnicity, incident chlamydia, sex with an IDU partner and receipt of money/items/drugs for sex.

† Any use of poppers, methamphetamine, dissociatives, hallucinogens, and/or cocaine.

‡ Urethral, thoracic and/or rectal.

§ Square root transformed.

by more than 85% in highly adherent MSM^[33,34] depending on social interactions and adherence patterns.^[35] We did not find any differences in adherence to PrEP among MSM with transgender partners compared with MSM not reporting

transgender partners. There has been discrepancy in reporting of risk behaviors between studies based in clinics versus clinical trials. Some clinic based studies suggest risky sexual practices such as condomless sex may be higher in populations on

Table 3**Adjusted/unadjusted odds of PrEP adherence for HIV-uninfected cis-MSM reporting ≥ 1 transgender sexual partner.**

			Adequate or perfect adherence ^a						
			Univariate			Multivariate			
	No (N=39)	Yes (N=319)	Tot [‡] (N=355)	OR	95% CI	P	AOR [†]	95% CI	P
Transgender sexual partner									
No	36	309	345	Ref	—	—	Ref	—	—
Yes	3	7	10	0.27	0.07–1.10	0.067	0.39	0.08–1.71	0.210

AOR=adjusted odds ratio, CI=confidence interval, MSM=men who have sex with men, OR=odds ratio, PrEP=pre-exposure prophylaxis, TDF-DP=tenofovir diphosphate.

^a Adequate or perfect adherence is measured by TDF-DP levels >719 fmol/punch (≥ 4 doses/week).^b Adjusted for race/ethnicity, education, receipt of money/items/drugs for sex, and sex with HIV positive, unknown or injection drug using partner.^c Missing adherence results for 37 (9%) participants.

PrEP^[36,37] facilitating transmission of STIs, which was different than prior clinical trials of PrEP that did not show such evidence.^[33,35] In our cohort, frequency of condom use for insertive or receptive anal sex were not associated with having transgender partners. Our results did not identify a significant difference between number of cis-male partners over 48 weeks and MSM with and without transgender partners, suggesting MSM on PrEP overall do not engage any differently with other cisgender male partners regardless of reporting a transgender partner. This finding is different than HPTN cohort where African American MSM with transgender partners had ≥ 5 new partners (AOR 3.67, 95% CI 2.98–4.97) in the last 6 months before data collection.^[15] A reason for the differences may be due to comparing behavior over time versus at baseline, and a population of primarily White and Hispanic MSM on PrEP versus only African American MSM who are either HIV positive or negative in the HPTN trial. Despite this difference, our results also show MSM with transgender partners may play a critical role in the transmission between the 2 groups.^[12,15,30]

Our analysis has several limitations. As we performed a secondary analysis of a PrEP trial, only the main study was sufficiently powered and only a small number of MSM reported a transgender partner, restricting confounders to adjust for in the multivariable model and conducting sub-group analysis between TGW and TGM. Our questionnaire did not explicitly distinguish between casual versus primary sexual partners, however, 69% of the time the method to meet partner was through internet, mobile applications, bath house, bar, sex party or other, suggesting this cohort were possibly engaging more with casual sexual partners. Our results may not be generalizable to all MSM in southern California, since MSM enrolled in the main study were at increased risk for HIV and other STI than the general MSM population. Moreover, as cisgender males reporting TGW or TGM partners may not identify as either gay or MSM, our results do not address this gap in gender identity and may not be generalizable to all MSM. Finally, as PrEP was provided for free to participants in the main study, we are unsure how interruption in PrEP uptake beyond the study period may affect these behaviors. Despite these limitations, our study used longitudinal data to study behavior of high-risk MSM on PrEP identifying risk behaviors that may change over time and sociodemographic factors associated with having a transgender partner.

Our results show MSM with transgender partners have higher HIV risk behaviors compared with their non-transgender reporting counterparts. This finding reinforces the need to address the sexual networks of transgender people that include high-risk MSM and drivers that determine sexual partner

interactions such as the role of sex work, socioeconomic status, and social interactions. A comprehensive approach to HIV prevention in the transgender community incorporating structural interventions in health and human rights, education and economic opportunities to reduce the need for survival sex, along with clinical preventive interventions may be more beneficial and efficacious. Better understanding of this interaction may help in the design of new interventions or adaptation of existing strategies to meet the unique HIV prevention needs for those at-risk of HIV acquisition in the transgender community.

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